REMARKS

Claims 5, 7, 8, 13, 15 and 16 have been amended to correct the dependencies of those claims. No new matter has been added. Claim 1 has been cancelled without prejudice. Applicants reserve the right to pursue the cancelled subject matter in a continuing application.

Claims 2 and 5-16 are pending.

INTERVIEW SUMMARY

Applicants thank Examiners Ford and Tongue for the interview conducted with Applicants' representative on October 5, 2010 during which the Applicants described the invention and discussed claim 2. The Examiners also requested information as to whether the method described in claim 2 can be used to determine culture conditions in cells other than stem cells. Applicants explained that the split pool method as described in claim 2 allows cells to be subjected to a series of culture conditions and be exposed to a series of agents in culture media in a systematic and highly productive manner as further explained on p. 5, paragraph 3 of the specification. This method is particularly efficient because multiple cell units can share a single vessel where they can be cultured under identical conditions. See for example, the specification at p. 32. Further, the method can be carried out using only a few culture vessels at any one time. Id. The method can be used to sample growth or differentiation conditions for any cell type, or the efficiency of biomolecule production (e.g. production of erythropoietin or interferon) by any cell type. Id. For example, Example 1 describes a split-pool cell culture experiment to assay the tissue culture conditions for differentiation of ES cell units. See p. 41-45 of the specification. Example 2 describes a split-pool culture experiment to assay tissue culture conditions of HepG2 cell units. See p. 46-47 of the specification.

CLAIM REJECTIONS

Rejection of claims under 35 U.S.C. 103

The Examiner has rejected claims 1, 2 and 5-16 under 35 U.S.C. § 103(a) as being unpatentable over Nishikawa et al. (*Development*, 1998; Vol. 125, p. 1747-1757) ("Nishikawa"). See Office Action at p. 2. Not in acquiescence to the rejection but in an effort to expedite prosecution, claim 1 has been cancelled thus rendering this rejection moot with respect to claim 1. Claims 5-8, 10 and 12-16 depend from independent claim 2.

Claim 2 relates to a method for determining the effect of a plurality of culture conditions on a cell, that includes the steps of a) providing a first set of groups of cell units each including one or more cells, and exposing the groups to desired culture conditions, (b) pooling two or more of the groups to form at least one second pool, (c) subdividing the second pool to create a further set of groups of cell units, (d) exposing said further groups to at least one change of culture conditions, (e) repeating steps (b)-(d) iteratively and (f) assessing the effect on a given cell unit of the culture conditions to which it has been exposed.

As previously explained, Nishikawa describes that "CCE ES cells ... were initially maintained in Mitomycin C ... treated embryonic fibroblast layers in Dulbecco modified essential medium (DMEM: Gibco) ...." See p. 1748. Nishikawa further describes transferring ES cells "to gelatin (Sigma, USA)-coated culture dishes to remove fibroblasts." Id. Nishikawa also states that "10^4 ES cells were then transferred to each well of type IV collagen-coated 6-well cluster dishes ... and incubated in a-MEM supplemented with 10% FCS and $5X10^{-5}$M 2ME." Id. Nishikawa then describes harvesting the cells and analyzing cells for surface markers. Id. Nishikawa does not teach or suggest that groups of cell units are pooled and then further sub-divided prior to exposure to at least one change of culture conditions and furthermore, that the steps of pooling and sub-division are repeated iteratively. See claim 2.

In Nishikawa, the initial step of growing the ES cells on mitomycin C treated embryonic fibroblasts layers is undertaken to **maintain** the cells as ES cells and not as part of a method for determining the effect of a plurality of culture conditions on a cell (see p. 1748). Furthermore, as indicated by the final paragraph in the left-hand column on page 1748, the transfer of the ES cells to gelatin is undertaken to **remove fibroblasts** and as such, cannot in any way be considered to be part of a method as claimed in claims 1 or 2 because this transfer is not directed towards a method for determining the effects of culture conditions on a cell. This transfer step is merely directed towards producing cells which are suitable as the starting material for subsequent use in Nishikawa. This position is further supported by the first sentence in the right-hand column of page 1748 which indicates that following the transfer of cells to gelatin-coated culture dishes, the cells are still considered to be ES cells. These ES cells are then transferred to type IV collagen coated 6-well culture dishes. Id.

The skilled person viewing Nishikawa would understand that it is these ES cells which must be considered to be the first set of cell units referred to in step (a) of claim 2. The cells are

then exposed to medium comprising α-MEM supplemented with 10% FCS and 2 ME. Id. Subsequently, these cells are analyzed for the expression of surface markers. Id. In a different experiment, the cells were incubated in medium containing a mixture of recombinant growth factors. Id. Therefore, Nishikawa does not only not disclose repeating the steps of claim 2 iteratively, but does not even disclose the step of pooling and sub-dividing one or more of said groups to create a further set of groups of cell units which are subsequently exposed to at least one change of culture conditions.

It is not obvious to one of ordinary skill in the art to modify the teaching of Nishikawa to result in a method which includes repeating steps corresponding to steps (b)-(d) of claim 2 iteratively. Nishikawa is directed towards the production of specific cell types in 2D culture (see p. 1748), not to the regulation of cellular processes through modulation of culture conditions and so would not provide a motivation for the skilled person to undertake any such experimentation. In fact, Nishikawa teaches away from modifying or changing the culture conditions as Nishikawa indicates that the conditions disclosed in Nishikawa are effective.

As such, Nishikawa does not teach or suggest a method for determining the effect of a plurality of culture conditions on a cell, that includes the steps of a) providing a first set of groups of cell units each including one or more cells, and exposing the groups to desired culture conditions, (b) pooling two or more of the groups to form at least one second pool, (c) subdividing the second pool to create a further set of groups of cell units, (d) exposing said further groups to at least one change of culture conditions, (e) repeating steps (b)-(d) iteratively and (f) assessing the effect on a given cell unit of the culture conditions to which it has been exposed.

Accordingly, claim 2 and claims that depend therefrom are patentable over Nishikawa. Applicants respectfully request that this rejection be reconsidered and withdrawn.

CONCLUSION

Applicant believes that the claims are in condition for allowance. A petition for an extension of time and a Request for Continued Examination are attached. Should any further fees be required by the present Reply, the Commissioner is hereby authorized to charge Deposit Account 19-4293.

Respectfully submitted,

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